

### **Neurosteroids: A New Regulatory Function in the Nervous System.**

Baulieu E-E, Robel P, Schumacher M, editors. Totowa (NJ): Humana Press; 1999. 378 pp with index. ISBN 0-89603-545-X (cloth). US\$135.

One of the more astonishing and pleasurable aspects of science is the way we are constantly surprised. Steroids are molecules well known since the early part of the last century; they had become rather unfashionable by the late 20th century, though drug companies developing new contraceptives retained an interest. But it was difficult to find a research lab still measuring steroids.

Several recent developments in neuroscience have changed all that. The emerging role of many steroids, particularly the glucocorticoids, in brain damage or malfunction (e.g., depression), is one factor; many groups worldwide are working on ways to limit acquired damage or age-related degeneration by using steroids or compounds that interfere with their action. One of the “givens” of steroid biology was that they were lipid-soluble compounds secreted from peripheral endocrine organs; their effects on the central nervous system therefore were dependent on passage across the blood-brain barrier and subsequent binding to macromolecular receptors in steroid-sensitive areas of the brain.

Then, it became apparent that the brain was able to modify these steroids in regionally specific ways, producing metabolites that were themselves highly active. Some call this an example of “intra-

crinology.” So, regional control of these processes became a focus of great interest — for example, how did the enzymes responsible change during development or under defined environmental conditions (e.g., the cortisol–cortisone shuttle, conversion of testosterone to estrogenic compounds, processing of progesterone to ring A saturated compounds)?

This was startling enough, but another surprise was on its way. Work by a number of groups, particularly those from whom these editors derive, established that the brain not only responds to and modifies steroids, it also makes them. Of course, this finding, when first presented, aroused fierce controversy (as all new ideas are bound to do). It turned conventional ideas on their heads because, if the brain can make steroids, how can we predict the role they may play in neuroendocrine function (or psychopathology) by simply measuring levels in the blood? What role do locally made steroids play in these functions? Under what conditions are they altered? How do we relate the activities of local steroids to those entering the brain from the more conventional bloodborne route?

Though there have been many reviews of neurosteroids, as these compounds have become known, this is the first book devoted to them. It benefits from great authority: all those whose work has been prominent in this new, and still disputed, field are represented here. The first chapter, by Robel, Baulieu and Schumacher, is a clear account of what we mean by the

term “neurosteroid” and a summary of our current knowledge of their variety and disposition in the brain. Read this chapter to update yourself; it’s comprehensive without being overbearing, as you might expect from leaders in this field. Even the often tortuous etymology of steroids and their enzymes is treated clearly and well.

Mellon and Compagnone, who have been prominent in defining the way that neurosteroids alter during development, give an extremely comprehensive, but entirely comprehensible, account of this work. Inevitably, at such an early stage in this research, many unanswered questions are raised. But they are fascinating ones, bearing in mind what we already know of the potent effects that some steroids can have on developmental processes (e.g., the role of prenatal testosterone on subsequent sexual behaviour). How many other steroids play so critical a role?

Warner and Gustafsson, also well-known workers, provide an excellent, highly focused account on just 1 enzyme: P450. This enzyme turns out to have many forms and functions, and tracing these in the brain provides a great detective story. Again, one senses that much of the true significance of this work remains for future studies to reveal.

There follow several shorter chapters, each focusing on a particular aspect of steroid catabolism. Caron et al tell us about steroidogenic factor 1, though some of their work is on peripheral tissues. Cascio et al give an account of the

peripheral-type benzodiazepine receptor (PBR); some of their information can be related to that provided in earlier chapters. Conversion of parent steroids by the brain, as we have said, is now recognized as an essential process. Poletti et al focus on several important examples (i.e., aromatases, reductases and oxidoreductases). This is an up-to-date and readable account.

One of the most interesting aspects of neurosteroids for neurologists and psychiatrists is the fact that they interact with classical receptors, including the GABA<sub>A</sub> receptor. Lambert et al describe this, and Purdy and Paul add weight. Majewska, who has been prominent in this area as well, suggests direct relations between neurosteroids and brain function (e.g., mood). The theme is continued by Gibbs et al, who discuss interactions with glutamate receptors, and Bastianetto et al tackle the difficult topic of the somewhat mysterious sigma receptors, somehow involved in neurosteroid actions in the brain. The wide-ranging actions of neurosteroids is emphasized by Buisson and Bertrand, who discuss their action on the ubiquitous glutamate receptor, whilst French-Mullen tells us that neurosteroids also act on voltage-gated Ca<sup>++</sup> channels (another fundamental property).

If, by now, you still need convincing that these are molecules of extraordinary interest, read the chapter by McEwen, who brings much of the preceding discussion together in his account of the actions of estrogens on the brain. The theme of neurosteroids in pathology is continued by Garcia-Segura et al in an excellent chapter on the way that these steroids modulate

brain plasticity both during development and after injury.

The interaction between neurosteroids and receptors in the cell membrane, implicit in previous chapters, is explored in detail by Ramirez and Zheng; they focus on estrogens. This theme is further developed by Toran-Allerand, who tells us much, particularly about the interplay between estrogens and growth factors (a second set of topical molecules in the brain). Lest we forget that all this has to have functional significance, Mayo et al focus on the behavioural actions of neurosteroids (particularly on aggression and memory, 2 topics of immense importance), and Roberts, a pioneer in this area, continues the theme in his chapter. Is this the therapeutic future for these compounds? Finally, Rupprecht et al discuss the neuropharmacology of some neurosteroids, particularly DHEA, progesterone and pregnenolone.

This book avoids most of the usual pitfalls of multiauthor volumes: it has a theme, contemporary and relatively unexplored, and the chapters are well constructed, relevant and don't overlap too much. Packed with digestible information, it fully justifies its title. We are on the threshold of a new branch of neuroscience, and this is our travel guide.

**Joe Herbert, MB ChB, PhD**  
Cambridge, United Kingdom

**Treatment Plans and Interventions for Depression and Anxiety Disorders.** Leahy RL, Holland SJ. New York: The Guilford Press; 2000. 332 pp with index. ISBN 1-57230-514-2 (paper and CD-ROM). US\$55.

This book is one of the latest additions to the *Clinician's Toolbox* series from Guilford Press. It is written by 2 psychologists with a wealth of experience in providing cognitive behaviour therapy (CBT) to individuals suffering from depression and anxiety disorders, as well as in training clinicians to administer CBT. The authors have also published several other practical books on cognitive therapy for practitioners.

Leahy and Holland provide step-by-step CBT protocols, adapted from manuals that have been extensively tested at research centres around the world. The protocols are written for the clinician who may be constrained with respect to the number of sessions that he or she can offer, as well as by the length of time available for each session.

The first chapter provides an overview of issues related to CBT in managed care settings. The 7 chapters that follow provide treatment plans for particular syndromes, including depression, panic disorder and agoraphobia, generalized anxiety disorder, social phobia, post-traumatic stress disorder, specific phobia, and obsessive-compulsive disorder.

The structure of chapters 2 through 8 is similar; each begins with a description of the disorder in question and suggestions for differential diagnosis. The authors review behavioural and cognitive models for the disorder, provide information regarding other contributing factors and briefly review the research on cognitive behavioural treatments for the disorder. An overview of assessment and treatment strategies is provided next, followed by a case example